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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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EXAMINER

HM11/0724

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ART UNIT	PAPER NUMBER
1646	5

DATE MAILED: 07/24/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-21 is/are pending in the application.
Of the above, claim(s) 20-21 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-19 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 1-21 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3
☐ Interview Summary, PTO-413
☒ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

* U.S. GPO: 1998-404-496/

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-19, drawn to an isolate DNA, vectors, cells, a method of making a polypeptide, a polypeptide and a composition, classified in class 435, subclass 69.1.

   II. Claims 20-21, drawn to an antibody, classified in class 530, subclass 387.1.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related to different products. Although there are no provisions under the section for "Relationship of inventions" in MPEP806.05 for inventive groups that are directed to different products, restriction is deemed to be proper because these products appear to constitute patentably distinct inventions for the following reasons:

Groups I-II are directed to products that are distinct both physically and functionnally, and are therefore patentably distinct. The nucleic acids of invention I are independent and distinct from the antibody of Group II , while each product can be made independently from the other and used for different purposes.

The proteins of invention I are related to the antibody of invention II by virtue of being cognate antigens, which may be used for the production of the antibodies. Although the protein and antibody are related due to the necessary stearic complementarity of the two, they are distinct

inventions because they are physically and functionnally distinct chemical entities, and because the proteins can be used in other and materially different processes from the use for production of the antibody, such as in pharmaceutical compositions, or in a diagnostic assay.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, and because the searches required for each of the groups are different, restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Anne Perkins on 1/7/98, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-19. Affirmation of this election must be made by applicant in responding to this Office action. Claims 20-21 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

6. A CRF error has been corrected by the STIC Systems Branch: they deleted *ending* stop codon in amino acid sequence (SEQ ID No:2).

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 2, 4, 5, 18, and their dependent claims are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As discussed in the rejection under 35 U.S.C. 112, second paragraph, below, claims 1, 4, 5 and 18 are indefinite. Given that the metes and bounds of the claims cannot be determined, it follows that, without knowing what an "AIR" polypeptide is, one cannot make a number of species of such commensurate inscope with the claims, nor determine how to use such.

Furthermore, regarding claim 4, 5 and 18, as the AIR polypeptide might comprise SEQ ID No:2 *plus* an extra amino terminus and/or an extra carboxy terminus, or might be any polypeptide

having an amino terminus and a carboxy terminus selected from SEQ ID No:2, and as the claims read on the amino terminus and carboxy terminus consisting of "an" amino acid, one of skill in the art would not know how to use a polypeptide having for example SEQ ID NO:2 to which are fused an amino acid from position 1-29 and an amino acid from position 190-200.

Claim 2 recites a nucleotide sequence derived from the DNA of SEQ ID No:1. Such a sequence can include for example nucleic acid with chemical modifications, modified bases, biotynilated molecules, and basically any possible nucleic acid sequence. One of skill in the art would not know how to make such molecules commensurate in scope with the claim, and how to use them.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-3, 6-7, 10-11, 13-14, 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 3 are indefinite, because they recite the amino acid sequence of SEQ ID No:5, while the sequence listing indicates SEQ ID No:5 as being a nucleic acid.

Claim 1 is indefinite, because it recites a DNA encoding a protein named AIR, and that the name of a protein does not define it in terms of structure or function. Others in the field may isolate the same protein and give such an entirely different name. In fact, the name of a protein is arbitrarily

assigned by the inventors thereof, and may change over time as more is discovered about the protein. For example, interleukin-1 is also known as lymphocyte activating factor, endogenous pyrogen, leucocyte endogenous mediator, mononuclear cell factor, and catabolin (see Callard et al, The Cytokine FactsBook, Academic Press Ltd, 1994, page 31).

Claim 1 is further indefinite, because it recites DNA capable of hybridizing under stringent conditions , and while the specification gives an example of the conditions described as stringent at page 10, lines 10-11, the specification cannot be read into the claims . Furthermore, the conditions described as stringent in the specification, page 10, lines 10-11, would not allow to discriminate between the molecule of the invention and other unrelated molecules. For example, a wash performed in 3XSSC at 55 degree C would allow non-related molecules to hybridize, because the high salt concentrations offsets the stringency conferred by the temperature.

Claim 1 is further indefinite, because it recites biologically active AIR, and while the specification refers to AIR activity, page 4, lines 31-34, "biologically active AIR" is not so defined as to adequately define a function peculiar to AIR. For example, a biological activity of AIR could be to be cleaved by a peptidase or to generate an immune response. Moreover, biologically active fragments would also embrace epitopes for antibodies, and such an epitope could not be used in accordance with the invention.

Claim 2 is indefinite, because it is not clear what is meant by " a nucleotide sequence derived from the DNA of SEQ ID NO:1", and that the metes and bounds of "derived" are not provided.

Furthermore, a fragment of 17 nucleotides or 30 nucleotides is far too short to encode the cytoplasmic domain of AIR, discosed at page 5, line 24, as being a 193 amino acid cytoplasmic tail.

Claims 3, 16, 17, 18 are rejected over the terms of "biologically active AIR", "biologically active fragments", and "stringent conditions" for the reasons discussed in the rejection of claim 1, *supra*.

Claims 3 and 17 are are indefinite with respect to a polypeptide at least about 70% identical to another polypeptide. The Examiner takes note that applicants refer to how a percent identity may be determined, page 9, lines 26-30. However, the level of sequence identity is dependent upon the type of analysis used for the sequence comparison. The specification does not disclose how to calculate the percent identity, like for example which parameters are set (i.e. gap penalties, mismatch penalties, etc...). Thus, the specification does not teach the type of sequence comparison used such that one skilled in the art can determine what is meant by 70% identity. As taught by George et al., Macromolecular sequencing and synthesis, Alan Riss , p. 127-149, 1988, "the results of the analysis are entirely dependent on the choice of scoring rules" (p. 130, col.2, lines 4-6). Thus, absent a knowledge of the type of sequence comparison and scoring rules that is used to determine 70% identity, the metes and bounds of the claims cannot be determined. Furthermore, it is not clear what the metes and bounds of "at least about 70%" are.

Claims 6-7, 10-11, 13-14 are rejected as dependent claims.

Claim 18, line 5, is missing the word "of" between "consisting' and "an".

Claims 13, 14 and 15 lack antecedent basis for "the AIR". Claims should be amended to recite " the AIR protein".

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-3, 6, 7, 10, 11, 13, 14, 16 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier et al., The WashU-Merck EST project, EST NCBI Accession H46211 or H46374, July 31, 1995 .

The EST fragment H46211 has stretches of for example 116 nucleotides identical to SEQ ID No:1 (position 90-205), and is overall 95.7% identical to SEQ ID No:1 from position 90-436 (see sequence comparison attached).

The EST fragment H46374 has stretches nucleotides of, for example, 21 nucleotides and 39 nucleotides identical to SEQ ID No:1 at positions 115-135 and 273-312 (see sequence comparison attached).

Such EST fragments encode a protein comprising biologically active fragments of AIR, like for example an epitope of AIR. It would have been obvious for one of skill in the art, and one would have been motivated to do so, to express an EST fragment in order to make an antibody useful for protein purification.

13. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Screaton et al., Proc Natl Acad.Sci USA 94(9):4615-19, April 1997, teach LARD, a lymphoid-specific death domain containing receptor (see sequence comparison attached).

Marsters et al., Curr.Biol., 6(12): 1669-76, December 1, 1996, teach Apo-3, a member of the TNF receptor family that contains a death domain and activates apoptosis (see sequence comparison attached) .

Chinnayian et al., Science 27495289):990-2, November 8, 1996, teach DR3, a death domain containing receptor related to TNFR-1 (see sequence comparison attached).

Bodmer et al., Immunity 6(1):79-88, 1997 teaches TRAMP, an apoptosis mediating receptor with sequence homology to TNFR-1 (see sequence comparison attached).

These results were published after the priority date of the provisional application 60/044456 (October 4, 1996).

Wiley et al., Immunity 3(6):673-82, December 1995, teach TRAIL, a type II membrane protein which is a member of the TNF ligand family. While soluble TRAIL induces apoptosis in some cells, no known member of the TNF receptor family binds to TRAIL.

Hartwell et al., US Patent 5,674,996, teach a sequence of 75 nucleotides that is 100% identical to SEQ ID No;1 (position 69-143), Example 4, col.41-46 (see sequence comparison attached).

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eliane Lazar-Wesley, PhD, whose telephone number is (703) 305 4059. The examiner can normally be reached on Monday-Friday from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached on (703) 308-2731.

Official papers filed by fax should be directed to (703) 308 4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.
ELW

July 15, 1998

ELW

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER